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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,803	11/07/2001	Fernand Labrie	P/1259-637	3989
2352 7590 09/14/2007 OSTROLENK FABER GERB & SOFFEN 1180 AVENUE OF THE AMERICAS NEW YORK, NY 100368403			EXAMINER CHONG, YONG SOO	
			ART UNIT 1617	PAPER NUMBER
			MAIL DATE 09/14/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/052,803

Applicant(s)

LABRIE, FERNAND

Examiner

Yong S. Chong

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 June 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,13-19,22-24,35-41 and 44 is/are pending in the application.
- 4a) Of the above claim(s) 24 and 44 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,13-19,22,23 and 35-41 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>3/9/07</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of the Application***

This Office Action is in response to applicant's arguments filed on 6/27/2007. Claim(s) 3-12, 20-21, 25-34, 42-43 have been cancelled. Claim(s) 1-2, 13-19, 22-24, 35-41, 44 are pending. Claim(s) 24 and 44 have been withdrawn. Claim 1 has been amended. Claim(s) 1-2, 13-19, 22-23, 35-41 are examined herein.

Applicant's arguments have been fully considered but found not persuasive to withdraw the rejections. The rejections of the last Office Action are maintained for reasons of record and repeated below for Applicant's convenience.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Simard et al. (International Journal of Cancer (1997), 73(1 ), 104-112, "83" in PTO-1449 submitted November 7, 2001 ) for reasons of record stated in the Office Action dated February 8, 2005.

Simard et al. discloses a composition comprising 1713-estradiol (E2), the instant estrogen, and a simultaneous incubation with EM-652 or EM-800, the instant SERM compound, and a pharmaceutical diluent or carrier such as ethanol and water in vitro.

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See abstract, page 104-105; Fig 2-12 at page 106-111. Thus, the testing results show that EM-652 or EM-800 as non-steroidal antiestrogens are useful in treating breast cancer in patients (see abstract), particularly including those woman patients who need to take estrogens daily for hormone replacement therapy (HRT).

Claims 1-2 and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Couillard et al. ("8" in PTO-1449 submitted November 1, 2004) for reasons of record stated in the Office Action dated February 8, 2005.

Couillard et al. discloses that administering estrone, the instant estrogen, to mice while co-administering EM-800 and DHEA in a composition with a pharmaceutical diluent or carrier, is useful in inhibiting breast tumors or cancer growth in mice.

### ***Response to Arguments***

Applicant argues that the Simard and Couillard references do not disclose a "pharmaceutical dosage form." At the outset, there is no explicit limitation in the claims reciting a "pharmaceutical dosage form." Moreover, this is not persuasive because Simard clearly disclose ethanol as a pharmaceutical carrier (pg. 105, right col. 2<sup>nd</sup> paragraph), therefore rendering the composition in a finished form suitable for administration to a patient. With regard to the Couillard reference, Examiner notes that once the active agents are administered to a patient, the composition is in contact with water in the blood.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham vs John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 17-19, 22-23, and 35-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simard et al. or Couillard et al. for reasons of record stated in the Office Action dated February 8, 2005.

The same disclosure of Simard et al. or Couillard et al. has been discussed in the 102(b) rejection set forth above.

The prior art does not expressly disclose the employment of a kit to store the compositions of Simard et al. or Couillard et al. The prior art does not expressly disclose the employment of the known pharmaceutically acceptable salt of the acid in a pharmaceutical composition or a kit.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a kit for comprising the composition of Simard et al. or

Couillard et al. and to employ the known pharmaceutically acceptable salt of the acid in a pharmaceutical composition or a kit, since the patient pack or kit and the pharmaceutically acceptable salts are all deemed obvious; they are all within the knowledge and conventional skills of pharmacologist to conveniently assist the user and prescriber for easy dispensary of the medication.

Claims 1-2, 13-19, 22-23, and 35-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Luo et al. ("54", PTO-1449 submitted November 7, 2001) and Barrett-Connor et al. ("4", PTO-1449 submitted November 7, 2001), and Do Nascimento (of record) in view of Labrie et al. (WO 96/26201, PTO-1449 submitted November 7, 2001), for the same reasons of record in the Office Action dated February 8, 2005.

Luo et al. discloses that an estrogen, DHEA alone, or the particular SERM (antiestrogen), EM-800 alone (having 2S configuration and moieties convertible in vivo to hydroxyl), is known to be useful in a method of treating hyperlipidemia by decreasing serum lipid levels such as triglyceride and cholesterol levels. See abstract and page 4436 Fig. 1 "Structure of EM-800", page 4438 the left column "Effect on serum lipid levels". Luo et al. further discloses that the combination of DHEA and EM-800 exerts more potent effect on reducing serum lipid levels than each compound used alone (page 4438 the left column "Effect on serum lipid levels" and page 4439 Fig. 4, and page 4443 the left column.

Barrett-Connor et al. teaches that SERMs are capable of lowering serum lipid levels to reduce the risk of coronary heart disease, as estrogen does. See abstract.

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Do Nascimento teaches that the particular estrogen, 1713-estradiol, is useful in treating hypercholesterolemic patients (see abstract).

The prior art does not expressly disclose the employment of the combination of an estrogen such as 1713-estradiol and the particular SERM, EM-652.HCl, or further combining with DHEA in a pharmaceutical composition.

Labrie et al. (WO 96/26201) discloses that both EM-800 and EM-652 or EM-652.HCl are antiestrogens (SERMs), and EM-800 has moieties convertible in vivo to hydroxyl to become EM-652. Thus, EM-800 is a metabolite of EM-652, having the same functional property and activity.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ of the combination of an estrogen such as 1713-estradiol and the particular SERM, EM-652.HCl, or to further combine with DHEA, in a pharmaceutical composition.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the combination of an estrogen such as 1713-estradiol and the particular SERM, EM-652.HCl, or to further combine with DHEA, in a pharmaceutical composition, since estrogens such as 1713-estradiol and DHEA are well known in the art to be used in methods of treating hyperlipidemia by decreasing serum lipid levels such as triglyceride and cholesterol levels according to the cited prior art herein. Moreover, the particular SERM, EM-800, a known metabolite of EM-652 (convertible in vivo to hydroxyl to become EM-652), alone or in combination with an estrogen such as DHEA, is known to be useful in a method of treating hyperlipidemia by

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decreasing serum lipid levels such as triglyceride and cholesterol levels according to Luo et al.

Therefore, one of ordinary skill in the art would have reasonably expected that combining an estrogen such as 17 $\beta$ -estradiol and the particular SERM, EM-652.HCl, or further combining with DHEA, all known useful for the same purpose, i.e., treating hypercholesterolemia, would improve the therapeutic effects for treating the same disorder, hypercholesterolemia, and/or would produce additive therapeutic effects in treating the same. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) regarding combination inventions. It is considered prima facie obvious to combine two active composition components into a single composition to form a third composition useful for the very same purpose.

Further, the teachings of Luo et al. that the combination of DHEA and EM-800 exerts more potent effect on reducing serum lipid levels than each compound used alone clearly provides the motivation of the instant claimed method employing the combination of EM-652, 17 $\beta$ -estradiol and DHEA.

Furthermore, one of ordinary skill in the art would have been motivated to prepare a kit comprising the same composition because the preparation of a kit comprising a pharmaceutical composition is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

Thus the claimed invention as a whole is clearly prima facie obvious over the teachings of the prior art.



***Response to Arguments***

Applicant argues "both Simard and Couillard teach against estrogen.

Couillard notes at abstract lines 6-7, "Estrone caused a 10-fold increase in ZR-75-1 tumor area..." ZR-75-1 is defined as human mammary tumor. Likewise, Simard states that estrogens play a predominant role in the development and growth of human breast cancer..." (Abstract, lines 1-2).

Applicant's argument is not found persuasive. Since first, the instant claims are directed to a pharmaceutical composition, which is a product claim not method claim. Thus, so long as Simard et al. discloses a composition comprising 17 $\beta$ -estradiol (E2), the instant estrogen, and a simultaneous incubation with EM-652 or EM-800, the instant SERM compound, and a pharmaceutical diluent or carrier such as water in vitro, or Couillard et al. discloses that administering estrone, the instant estrogen, to mice while co-administering EM-800 and DHEA in a composition with a pharmaceutical diluent or carrier, the prior art anticipates the claimed composition.

Second, as set forth in MPEP 2131.05, "Argument that the alleged anticipatory prior art is 'nonanalogous art' or 'teaches away from the invention' or is not recognized as solving the problem solved by the claimed invention, [are] not 'germane' to a rejection under section 102" (see also *Twin Disc. Inc. V. United States*, 231 USPQ 417, 424 (Ct. Cl. 1986). The question whether a reference "teach away" from the invention is inapplicable to an anticipation analysis (see also *Celeritas Technologies Ltd v. Rockwell International Corp.*, 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1999).

Thus, in this case, Applicant's argument that "both Simard and Couillard teach against estrogen" is not germane to the 102 rejections herein.

Applicant argues that Luo does not disclose an estrogen. This is not persuasive because Luo clearly discloses estrogens.

Applicant also argues that Barrett-Conner does not test the presently-claimed SERMs on cholesterol. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., testing of the presently-claimed SERMs on cholesterol) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Therefore, one of ordinary skill in the art would have reasonably expected that combining an estrogen such as 1713-estradiol and the particular SERM, EM-652.HCl, or further combining with DHEA, all known useful for the same purpose, i.e., treating hypercholesterolemia, would improve the therapeutic effects for treating the same disorder, hypercholesterolemia, and/or would produce additive therapeutic effects in treating the same.

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... The idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

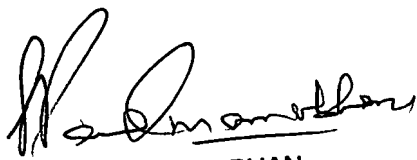
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC



SREENI PADMANABHAN  
SUPERVISORY PATENT EXAMINER